UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

In re APELLIS PHARMACEUTICALS, INC. SECURITIES LITIGATION	Case 1:24-cv-11470-JEK **ORAL ARGUMENT REQUESTED**

MEMORANDUM OF LAW IN SUPPORT OF DEFENDANTS' MOTION TO DISMISS COMPLAINT

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Defendants Apellis Pharmaceuticals, Inc. ("Apellis" or the "Company") and Dr. Cedric Francois (together with Apellis, "Defendants") respectfully submit this memorandum in support of their motion to dismiss the Amended Complaint (the "Complaint" or "¶ __").

INTRODUCTION

Apellis is a Massachusetts-based biopharmaceutical company that has developed pegcetacoplan, commercially referred to as SYFOVRE. In February 2023, the U.S. Food and Drug Administration ("FDA") approved pegcetacoplan for the treatment of geographic atrophy ("GA"). GA is an advanced form of age-related macular degeneration ("AMD"). Although there were no incidents of vasculitis—a form of inflammation of retinal blood vessels that can lead to blindness—observed in any of pegcetacoplan's clinical trials, in July 2023 an organization of retina specialists published a letter indicating that physicians reported six post-approval incidents of vasculitis in patients treated with pegcetacoplan (in the context of 60,000 vials that had been distributed to that point in time). In consultation with the FDA, a warning concerning vasculitis was added to the label. From this, Plaintiffs seek to concoct a claim of securities fraud. They allege that Defendants knew all along, but never disclosed, that pegcetacoplan was bound to cause vasculitis; and that the lack of observed cases during the clinical trials was misleading because Defendants designed the trials to avoid detecting it and/or should have known that patients were dropping out because of it.

As set forth below, the Complaint fails to allege securities fraud. First, all of Defendants' statements about the absence of observations of vasculitis in the clinical trials were truthful and in no way implied there was no risk that vasculitis might occur post-approval (and in fact warned to the contrary). The Complaint's after-the-fact criticisms of the protocols used in those trials, based on nothing more than the opinion of a single clinician, and without any supporting evidence such as from Company witnesses or documents, is inactionable scientific disagreement.

And the argument about dropouts is pure speculation. Second, and equally fatal, Plaintiffs offer nothing to establish the required cogent and compelling inference of scienter. Faced with no motive to commit fraud and no admissions, witnesses, documents, or other facts suggesting scienter, the Complaint instead principally relies on statements about different issues made after the alleged class period and suggest those somehow show scienter on the apparent theory that Defendants habitually lied. Not only is this insufficient, but the post-class period statements in fact were true and not misleading. As to the challenged statements themselves, the only plausible inference is innocent: that Defendants truthfully reported there were no observed incidents of vasculitis during the trials, had no intent to mislead, and a few incidents emerged post-approval when a substantially larger number of injections were given. For these and the other reasons set forth below, the Court should dismiss the Complaint with prejudice.

BACKGROUND

Apellis is a biopharmaceutical company based in Waltham, Massachusetts. ¶¶ 2, 24. Pegcetacoplan is a targeted therapy designed to regulate excessive activation of a part of the body's immune system, which can lead to onset and progression of serious diseases. ¶¶ 36-37. During the putative class period, Apellis conducted two Phase 3 studies—DERBY and OAKS—comparing the efficacy and safety of pegcetacoplan with sham injections in patients with GA. ¶ 40. GA is an advanced form of AMD, a leading cause of blindness. ¶¶ 34-35. In February 2023, the FDA approved pegcetacoplan for the treatment of GA secondary to AMD. ¶¶ 38-39.

Following FDA approval and the commercialization of pegcetacoplan, on July 15, 2023, the American Society of Retina Specialists ("ASRS") published a letter indicating that physicians had reported six incidents of retinal vasculitis in patients treated with pegcetacoplan. ¶ 9. Retinal vasculitis is a form of inflammation of retinal blood vessels that can lead to blindness. ¶¶ 43, 46, 49. These six incidents of vasculitis were observed after approximately

60,000 vials of pegcetacoplan had been distributed, which the Company estimated to have equated to a rate of roughly 0.01% incidents of vasculitis per injection. ¶ 133. No cases of vasculitis had been observed in DERBY or OAKS, in which approximately 23,000 injections were made. ¶¶ 77, 141. Apellis continued to track and report to the FDA and investors additional cases of vasculitis as they were reported. ¶¶ 114, 141-44. In fact, few additional cases of vasculitis were reported following the letter, and the rate of vasculitis per injection remained the same. *Id.* Consistent with the rarity of these events, the FDA did not withdraw approval of pegcetacoplan, recall any lots of the drug, or require a black box warning (the most serious warning to alert consumers about serious or life-threatening side effects).[1] Instead, in November 2023, the label for pegcetacoplan was simply updated to include a warning concerning vasculitis in addition to other known side effects. ¶ 116.[2] Likewise, consistent with the low risk of vasculitis, pegcetacoplan has been widely accepted by physicians, and Apellis has reported sales of over 100,000 vials of pegcetacoplan. *See* Ex. 1 at 9.

Seeking to manufacture fraud claims from these few unexpected post-approval incidents of vasculitis, Plaintiffs filed the Complaint on February 8, 2024, challenging numerous truthful statements Defendants made about the absence of observed vasculitis in its clinical trials over the course of 3 ½ years. The putative class period begins on January 28, 2021 (when Apellis commented on the results of the Phase 2 FILLY study and reported that it expected top line results from DERBY and OAKS in Q3 2021), ¶¶ 1, 76, and ends on July 28, 2023 (the day before Apellis provided an update on observations of vasculitis), ¶¶ 1, 15, 16. The Complaint brings claims against the Company and the Company's Chief Executive Officer, Dr. Francois,

[1] *See Lungu v. Antares Pharma Inc.*, No. 21-1624, 2022 WL 212309, at *1 n.3 (3d Cir. Jan. 25, 2022).
[2] Implicitly, the FDA had determined that the fundamental benefit-risk profile had not changed.

under Section 10(b) of the Exchange Act and Rule 10b-5 thereunder, and against Dr. Francois as a "control person" under Section 20(a).

The Complaint asserts that Defendants' truthful statements that no vasculitis was observed in DERBY and OAKS—and one early statement about the expected timing of top line results in the trials—were nonetheless misleading because (i) Defendants allegedly omitted to disclose that there was an "inherent" risk that pegcetacoplan would cause vasculitis based on its similarities to other treatments for which vasculitis was observed, or (ii) vasculitis allegedly had occurred during DERBY and OAKS but went unobserved because of the design of the trial protocol or patients dropping out from the study. *See, e.g.*, ¶¶ 79, 81, 83, *et seq.* This sort of second-guessing and manufactured falsity in hindsight fails to establish securities fraud.

ARGUMENT

I. Legal Standard

To state a claim under Section 10(b) and Rule 10b-5, a plaintiff must adequately plead: (1) a material misrepresentation or omission, (2) scienter, (3) a connection between the misrepresentation or omission and the purchase or sale of a security, (4) reliance, (5) economic loss, and (6) loss causation. *See ACA Fin. Guar. Corp. v. Advest, Inc.*, 512 F.3d 46, 58 (1st Cir. 2008). A complaint asserting securities fraud must comply with both the heightened pleading standards of Fed. R. Civ. P. 9(b) and the stringent procedural requirements of the Private Securities Litigation Reform Act of 1995 ("PSLRA"). *See In re Bos. Sci. Corp. Sec. Litig.*, 686 F.3d 21, 27, 30 (1st Cir. 2012). The PSLRA requires that a complaint "specify each statement alleged to have been misleading [and] the reason or reasons why the statement is misleading." *ACA Fin. Guar. Corp.*, 512 F.3d at 58 (internal quotation marks omitted).

The PSLRA similarly imposes a "rigorous pleading standard" for allegations of scienter. *Id.* "A complaint will survive a motion to dismiss only if it states with particularity facts giving

rise to a 'strong inference' that defendants acted with a conscious intent 'to deceive or defraud investors by controlling or artificially affecting the price of securities' or 'acted with a high degree of recklessness.'" *Fire & Police Pension Ass'n of Colorado v. Abiomed, Inc.*, 778 F.3d 228, 240 (1st Cir. 2015) (internal citations omitted). In the First Circuit, recklessness "does not include ordinary negligence, but is closer to being a lesser form of intent." *Id*. (*citing Greebel v. FTP Software, Inc.*, 194 F.3d 185, 188 (1st Cir. 1999) (internal quotation marks omitted)). Scienter is adequately pled "only if a reasonable person would deem the inference of scienter cogent and at least as compelling as any opposing inference one could draw from the facts alleged." *Tellabs, Inc. v. Makor Issues & Rights, Ltd.,* 551 U.S. 308, 324 (2007).

II. The Complaint Fails to Identify an Actionable Misstatement or Omission

A. The Complaint Does Not Allege that Any Statement Made During Apellis's January 2021 Investor Event Was False or Misleading

Plaintiffs challenge Defendants' truthful report in January 2021 that FILLY had met its primary endpoint and that the Company expected to report top-line results for DERBY and OAKS in Q3 2021. ¶ 76. The Complaint groups this statement with two others made over eight months later regarding the absence of observed vasculitis in DERBY and OAKS and asserts that the January 2021 statements are misleading for the same reasons. ¶ 79. The Complaint offers no explanation how the January 2021 statements were rendered misleading by omitting the alleged "inherent" risk of vasculitis or the details of DERBY and OAKS, the results of which were not yet available in January 2021. It was simply an inactionable opinion about timing. *Omnicare, Inc. v. Laborers Dist. Council Const. Indus. Pension Fund*, 575 U.S. 175, 185-86 (2015) (opinion only actionable if not sincerely believed or if supporting facts provided are untrue). Moreover, "[d]isclosure is required . . . only when necessary to make . . . statements made, in the light of the circumstances under which they were made, not misleading." *Matrixx Initiatives,*

Inc. v. Siracusano, 563 U.S. 27, 44 (2011) (internal quotation marks omitted). *When* Apellis expected top line results indicated nothing about the risk of vasculitis and could not have misled investors concerning that risk. The inclusion of this statement appears to be a transparent effort to push back the start of the alleged class period to claim more damages.

B. The Complaint Fails to Plead Contemporaneous Facts Showing Falsity

With respect to all statements other than those in January 2021, the Complaint challenges Defendants' reporting that vasculitis was not observed in DERBY and OAKS. The Complaint does not and cannot allege that these statements were false. Instead, it asserts that these true statements were misleading because Apellis did not disclose the alleged "inherent" risk of vasculitis, that subjects may have dropped out due to undetected vasculitis, and details of its trial protocol that was allegedly inadequately designed to detect vasculitis. *See* ¶¶ 79, 81, 83, *et seq.* None of these theories passes muster, and they betray an effort to fabricate falsity in hindsight.

1. The Complaint Fails to Plead Facts Establishing an "Inherent Risk of Vasculitis

The Complaint's only support for its allegation that there was "inherent" risk of vasculitis is that vasculitis has been observed with respect to other intravitreal injection treatments from other companies. *See, e.g.*, ¶¶ 52, 53-57 (specifically, Beovu). This fails to establish that the risk was inherent with pegcetacoplan, however, because it was, of course, a different drug. That other treatments caused vasculitis did not portend that pegcetacoplan would or that it would materialize at the same rate. *See, e.g.*, *Hou Liu v. Intercept Pharms., Inc.*, No. 17-CV-7371 (LAK), 2020 WL 1489831, at *8 (S.D.N.Y. Mar. 26, 2020) ("[E]ven if 'liver injury has been the most frequent single cause of safety-related drug marketing withdrawal over the past 50 years,' that is because the FDA took action against drugs other than Ocaliva manufactured by companies other than Intercept. This does not provide the requisite link between Ocaliva and the reported

adverse events or otherwise make the thirty SAEs material."); *see also In re Elan Corp. Sec. Litig.*, 543 F. Supp. 2d 187, 213-14 (S.D.N.Y. 2008) (rejecting claims based on notion that drug mechanism had an inherent risk because "[e]ven if scientists suspected that Tysabri might cause severe adverse events and Defendants knew of these suspicions, these facts would not have required Defendants to conclude that these effects were real before such a relationship was established").[3]

Moreover, Defendants' statements that vasculitis had not been observed in the trials did not imply (as Plaintiffs suggest) that there was *no* risk of vasculitis. To the contrary, it is obvious that Defendants were reporting on the absence of vasculitis precisely because it was potentially relevant. No one was misled. *See Backman v. Polaroid Corp.*, 910 F.2d 10, 16 (1st Cir. 1990) ("[R]evealing one fact about a product" does not mean one must reveal all facts, but only those "that are needed so that what was revealed would not be so 'incomplete as to mislead.'") (internal citation omitted); *Thant v. Karyopharm Therapeutics Inc.*, 43 F.4th 214, 225 (1st Cir. 2022) (given context and cautions, investors could not reasonably interpret statements to mean that drug was without significant adverse effects).[4] Indeed, Apellis also repeatedly disclosed the risk that adverse events not observed in DERBY and OAKS could materialize after commercialization of pegcetacoplan. Specifically, it warned:

> [C]linical trials by their nature utilize a sample of the potential patient population. However, with a limited number of subjects and limited duration of exposure, rare and severe side effects of our product candidates may only be uncovered when a

[3] Indeed, vasculitis associated with pegcetacoplan is much rarer than with Beovu. ¶¶ 136-39 (9-10 incidents per 10,000 injections for Beovu vs. 1 in 10,000 for pegcetacoplan). And Defendants had no reason to suspect that vasculitis would be an issue given that it was not observed during clinical trials.

[4] In addition, if the vasculitis associated with these other drugs was "high profile," as the Complaint alleges, it was obvious and did not need to be disclosed. *See Baron v. Smith*, 380 F.3d 49, 57 (1st Cir. 2004) ("It is not a material omission to fail to point out information of which the market is already aware.").

> significantly larger number of patients are exposed to the product. If safety problems occur or are identified after EMPAVELI or intravitreal pegcetacoplan or one of our other products, if any, reaches the market, the FDA or comparable non-U.S. regulatory authorities may require that we amend the labeling of such product, recall such product, or even withdraw approval for such product.[5]

This risk is precisely the one that materialized—a rare side effect that was not observed during DERBY and OAKS (which involved a limited cohort of patients receiving the treatment) but subsequently was observed in a few cases when pegcetacoplan was used in a much larger patient base after FDA approval. In that context, no reasonable investor would have understood Defendants to be claiming that there was no risk of vasculitis. To the contrary, investors would have understood exactly what Defendants said—that no actual cases had been observed during the trials, but that this did not guarantee there would be none observed post-marketing. Where, as here, issuers warn of the risk at issue, there is no actionable omission. *See, e.g.*, *In re The First Marblehead Corp. Sec. Litig.*, 639 F. Supp. 2d 145, 155 (D. Mass. 2009) ("A plaintiff fails to plead an actionable § 10(b) claim predicated on the concealment of information if that information was, in fact, disclosed.").[6]

The Complaint also notes that the rates of inflammation and neuropathy in DERBY and OAKS were similar to those of other intravitreal injection treatments associated with vasculitis. *See, e.g.*, ¶¶ 65, 79. But this leap of logic makes no sense: There is no factual predicate to assume these two types of adverse events portended a third. Moreover, Defendants repeatedly and accurately disclosed the adverse event rates and even noted that they were similar to the rates

[5] Ex. 2 at 59; *see also* Ex. 3 at 55 (similar); Ex. 4 at 55 (similar); Ex. 5 at 37 (referring investors to risk factors in 10-K).

[6] *See also Pizzuto v. Homology Medicines Inc.*, 1:23-CV-10858-AK, 2024 WL 1436025, at *8 (D. Mass. Mar. 31, 2024) (no misstatement where company "warned of the risk of inferring too much from . . . 'preliminary data,'" explaining that the "results should be 'viewed with caution'" as outcomes may change "when more data becomes available").

of other therapies.[7] *See, e.g.*, *In re Seadrill Ltd. Sec. Litig.*, 14 Civ. 9642 (LGS), 2016 WL 3461311, at *9 (S.D.N.Y. June 20, 2016) ("There can be no omission where the allegedly omitted facts are disclosed."). Defendants were not obligated to speculate further what this disclosed data might mean for the possibility of vasculitis, where vasculitis had not in fact been observed. That Plaintiffs may now have a different view does not establish fraud. *See Leavitt v. Alnylam Pharms., Inc.*, 451 F. Supp. 3d 176, 184 (D. Mass. 2020) ("Without specific allegations of falsity, opinions interpreting the results of a clinical study are not actionable."); *Leung v. bluebird bio, Inc.*, 599 F. Supp. 3d 49, 63 (D. Mass. 2022) (same); *Pizzuto*, 2024 WL 1436025, at *9 ("Courts have repeatedly held that interpretations of results of clinical studies are opinions.") (collecting authorities).[8]

[7] *See, e.g.*, Ex. 6 at 8 ("And the rates that we had in this study, which was 2 cases of infections, endophthalmitis, out of approximately 1,400 injections, was in line with other studies."); Ex. 7 ("Two cases of confirmed infectious endophthalmitis and one case of suspected infectious endophthalmitis were observed in the study eye out of a total of 6,331 injections (0.047%). Thirteen events of intraocular inflammation were observed in the studies (0.21% per injection)."); Ex. 8 at 4 (chart with neuropathy and inflammation data); Ex. 2 at 28 (similar); Ex. 9 at 17-18 (similar); Ex. 10 at 2 (similar); Ex. 5 at 24 (similar); Ex. 11 at 21, 24 (similar); Ex. 12 at 13 (similar); Ex. 13 at 6 (similar); Ex. 14 at 5 (similar); Ex. 15 at 5-7 (similar); Ex. 16; Ex. 4 at 9 (similar). All exhibits referenced herein ("Ex.") are attached to the Declaration of Dan Willey. Except the trial protocol discussed *infra* at n.17, these exhibits are all referenced in the Complaint. In ruling on a motion to dismiss, a court may consider "documents incorporated by reference in [the complaint], matters of public record, and other matters susceptible to judicial notice." *Lydon v. Local 103, Int'l Bhd. of Ele. Workers*, 770 F.3d 48, 53 (1st Cir. 2014) (internal quotation marks and citation omitted); *Harrington v. Tetraphase Pharm. Inc.*, No. CV 16-10133-LTS, 2017 WL 1946305, at *3 n.3 (D. Mass. May 9, 2017) (same). Defendants request that the Court take judicial notice of these press releases, filings, presentations, and analyst reports because each is referenced in the Complaint and central to Plaintiffs' claims (and several were filed with the SEC).

[8] Some courts addressing alleged omissions premised on scientific disagreement have analyzed them under *Omnicare*, 575 U.S. at 185-86, while others have analyzed the scientific disagreement on its own terms. Here, the Complaint does not allege that Defendants shared Dr. Vavvas's opinions about how the trial protocol should have been designed or allege that any facts Defendants cited in support of their statements of opinion were untrue. Thus, regardless of whether the Court applies *Omnicare*, the Complaint fails to state a claim.

2. The Complaint Fails to Plead Facts Establishing that Vasculitis Occurred in DERBY and OAKS

The Complaint's further assertion—which relies heavily on the opinions of a purported "expert," Dr. Demetrios G. Vavvas—is that there were in fact vasculitis events in DERBY and OAKS, but that they went undetected. This is entirely speculative and fares no better in establishing fraud. Dr. Vavvas does not furnish, and the Complaint does not otherwise identify, a single fact—from a document, witness, or otherwise—that demonstrates that vasculitis occurred during the trials but went undetected. Mere speculation that it *might have occurred* is plainly insufficient to establish falsity. *See, e.g.*, *Kader v. Sarepta Therapeutics, Inc.*, No. 1:14-CV-14318-ADB, 2016 WL 1337256, at *14 (D. Mass. April 5, 2016) (dismissing where "the bareness of the factual allegations makes clear that the plaintiff is merely speculating about the fact alleged and therefore has not shown that it is plausible that the allegation is true") (internal quotation marks and citation omitted). Moreover, the Court is not required to accept guesswork simply because it is packaged as expert opinion. *See Hershewe v. Joyy, Inc.*, No. 22-55377, 2023 WL 3316328, at *2 (9th Cir. May 9, 2023) (discounting conclusory expert opinions in pleadings in affirming dismissal); *In re Nektar Therapeutics Sec. Litig.*, 34 F.4th 828, 837 (9th Cir. 2022) (noting that "Plaintiffs cannot evade the PSLRA's exacting pleading standards by merely citing an expert who makes assertions about falsity based on questionable assumptions and unexplained reasoning" in affirming dismissal).[9]

That Dr. Vavvas' opinions are insufficient to establish a misleading statement, but instead are just speculation, is clear upon analysis. First, Dr. Vavvas supposes that vasculitis may have

[9] *See also Arkansas Pub. Emps. Ret. Sys. v. Bristol-Myers Squibb Co.*, 28 F.4th 343, 354 (2d Cir. 2022) ("[Expert] opinion cannot rescue the Investors' claims, unless that opinion was based on particularized facts sufficient to state a claim for fraud."); *Fin. Acquisition P'ners LP v. Blackwell*, 440 F.3d 278, 286 (5th Cir. 2006) ("[O]pinions cannot substitute for facts under the PSLRA.").

gone undetected because patients who experienced it may have dropped out of the studies rather than report their symptoms. *See* ¶ 8. The Complaint alleges, however, that vasculitis is a very serious adverse event that includes as a symptom *temporary or even permanent blindness*. *See, e.g.*, ¶¶ 5, 43-47. It defies logic that patients who experienced such symptoms would quietly drop out rather than report those symptoms and seek medical assistance.

Dr. Vavvas next speculates that vasculitis may not have been detected because angiography was required under the trial protocols only "at the end of the study" and not promptly if inflammation or neuropathy were observed. ¶ 7. According to Dr. Vavvas, had Apellis used a different protocol, and required earlier angiography, it might have detected cases of vasculitis that otherwise were treated or resolved by the time the protocol-required angiography was obtained. ¶ 65. To begin, Dr. Vavvas cites nothing in support of his assertion that angiography was obtained only at the end of the trial. In fact, as Apellis disclosed, angiography was assessed at baseline, months 12 and 24 of the studies, upon early termination, and also if new exudation related to development of active choroidal neovascularization[10] was suspected.[11] In any event, this is more speculation. Dr. Vavvas does not identify any actual cases of vasculitis that would have been detected with a different protocol. Dr. Vavvas also offers no facts about the rate at which vasculitis resolves itself sufficient to establish the likelihood that the protocol-specified angiography failed to detect cases for this reason.

[10] Choroidal neovascularization involves the growth of new, abnormal blood vessels that may leak and allow fluid to enter the retina, distorting vision.

[11] Ex. 17 at 36, 39-40, 72-83 (OAKS protocol). The Court may take notice of the protocol, which was (and is required to be) posted to clinicaltrials.gov, particularly where necessary to determine whether details of the trial were in fact omitted. *See, e.g.*, *Abely v. Aeterna Zentaris Inc.*, No. 12 Civ. 4711(PKC), 2013 WL 2399869, at *22 (S.D.N.Y. May 29, 2013) (taking notice of protocol posted to FDA site where complaint "asserts that the defendants misstated and omitted material aspects of the Phase 2 and Phase 3 trials," and review of such materials was "necessary to identify defendants' alleged misstatements and omissions, or lack thereof").

Moreover, setting aside what was required by the protocols, nothing prevented physicians from ordering angiography if they suspected vasculitis—which Dr. Vavvas admits would be sensible. *See, e.g.*, ¶ 48. If that angiography revealed vasculitis, it would be reported.

Moreover, the Complaint offers no explanation why the FDA would allow the clinical trial to proceed if the protocol was as flawed as Dr. Vavvas asserts. *See Lungu*, 2022 WL 212309, at *6 ("Given that the FDA approved the methods and procedures employed in the second clinical study, no reasonable investor would be concerned with patient enrollment data with which the FDA did not take issue.").[12]

Even leaving aside these fundamental factual and legal problems, Dr. Vavvas's opinion that more frequent angiography would have been better science and would have detected cases of vasculitis has a fatal legal problem: It at best establishes a non-actionable difference of opinion. *See Shash v. Biogen, Inc.*, 84 F.4th 1, 17 (1st Cir. 2023) ("[A] legitimate disagreement over scientific data does not give rise to a securities fraud claim . . . .") (internal quotation marks and citation omitted); *In re Karyopharm Therapeutics Inc., Sec. Litig.*, 552 F. Supp. 3d 77, 89 (D.

[12] *See also In re Phillip Morris Int'l Inc. Sec. Litig.*, 89 F.4th 408, 420-21 (2d Cir. 2023) ("We also have previously suggested in dicta – and now hold – that where the FDA eventually accepts a defendant's interpretation of the data, that interpretation is per se reasonable as a matter of law.") (internal quotation marks, alterations omitted); *In re Sanofi Sec. Litig.*, 87 F. Supp. 3d 510, 533 (S.D.N.Y. 2015) ("Had the FDA at any point concluded that there were 'serious defects in study design that would render the study incapable of producing valid evidence of safety and effectiveness,' it had 'authority to issue a clinical hold.'") (quoting 52 Fed. Reg. 8798).

Mass. 2021) (same).[13] Further, even if investors agreed with Dr. Vavvas, the details of the trial protocol were publicly disclosed—there was no omission.[14]

III. The Complaint Fails to Plead A Strong Inference of Scienter

Plaintiffs' failure to adequately plead scienter under the "rigorous" requirements of the PSLRA also requires dismissal. *See ACA Fin. Guar. Corp.*, 512 F.3d at 52, 67. The Complaint does not allege any facts demonstrating that Defendants consciously lied or were reckless as to the truth in making any challenged statement, and it bears none of the hallmarks typically supporting a strong inference of scienter. Instead, Plaintiffs (i) point to a handful of allegedly misleading post-class period statements to suggest illogically that if Defendants made such allegedly misleading statements after the purported class period, they must have also made the earlier challenged statements with scienter, and (ii) assert shop-worn "must have known" arguments such as "core operations" that this Court routinely rejects. The post class-period statements (which were not false or misleading, or about the clinical trials) fail to demonstrate anything about Defendants' state of mind with respect to the challenged statements; and without more, core operations allegations fail to establish scienter. Even considered holistically, these allegations fail to support an inference of scienter, much less one that is more compelling than the competing inference—that Defendants believed they were speaking truthfully and were not

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[13] *See also In re Keryx Biopharmaceuticals, Inc., Sec. Litig.*, Nos. 13 CIV. 755(KBF), 13 CIV. 1307(KBF), 2014 WL 585658, at *10 (S.D.N.Y. Feb. 14, 2014) ("[I]in scrutinizing a [false statement or omission] claim, a court does not judge the methodology of a drug trial."); *Abely*, 2013 WL 2399869, at *9 (citing *Kleinman v. Elan Corp., plc*, 706 F.3d 145 (2d Cir. 2013)) ("[D]isagreements over a study's methodology do not, standing alone, raise an inference of securities fraud.").

[14] The Complaint also quibbles with the way Apellis reported efficacy results based on a statistical model, ¶¶ 69-72, but does not actually challenge any of those statements. For the avoidance of doubt, the Complaint does not adequately allege that the statements are misleading, because Apellis clearly disclosed that the results it reported were based on a statistical model, and the Complaint's criticisms of that model are just more inactionable scientific disagreement.

misleading anyone when they reported that no vasculitis was observed in DERBY and OAKS, and that the low risk of vasculitis did not materialize until pegcetacoplan was used in a much larger patient base post-approval (which Defendants repeatedly warned might happen).[15]

A. The Complaint Does Not Allege Facts Showing that Defendants Knew or Were Reckless in Not Knowing That Any Statement Would Mislead

As an initial matter, the Complaint fails to adequately allege scienter because it is entirely devoid of the allegations courts typically rely on to find plaintiffs have met the PSLRA pleading standard—admissions, internal records or witnessed discussions suggesting that the defendants were aware that they were withholding material information. *See Yan v. Rewalk Robotics Ltd.*, 973 F.3d 22, 40 (1st Cir. 2020) ("In cases where [courts] have found the pleading standard satisfied, the complaint often contains clear allegations of admissions, internal records or witnessed discussions suggesting that at the time they made the statements claimed to be misleading, the defendant officers were aware that they were withholding vital information or at least were warned by others that this was so.") (internal quotation marks and citation omitted); *Shash*, 84 F.4th at 15 (affirming dismissal where "[i]nvestors' complaint lack[ed]" such allegations).

Securities plaintiffs also frequently attempt to bolster the inference of scienter through motive and opportunity allegations, such as suspicious insider trading whereby defendants profited from an inflated stock price, or other concrete personal benefits. *See, e.g.*, *Urman v. Novelos Therapeutics, Inc.*, 796 F. Supp. 2d 277, 283 (D. Mass. 2011); *Leavitt*, 451 F. Supp. 3d at 187–88. The Complaint is notably bereft of any of these types of motive allegations as well.

[15] Moreover, following ASRS's letter, Apellis voluntarily re-reviewed inflammation cases from the trials and confirmed that there were no vasculitis events (with additional external specialist re-review of severe cases), which further rebuts the inference that Defendants sought to hide vasculitis incidents from the trials. *See* Ex. 18 (July 29, 2023 press release cited at ¶¶ 15, 114).

Indeed, it does not point to *a single* suspicious insider trade. The absence of any allegation demonstrating knowledge, recklessness, or motive is fatal. *See Auto. Indus. Pension Tr. Fund v. Textron Inc.*, 682 F.3d 34, 39 (1st Cir. 2012) (affirming dismissal where "warnings by subordinates or expressions of concern by executives" were "notably absent"); *In re Bos. Sci. Corp. Sec. Litig.*, 686 F.3d at 31 (affirming dismissal where complaint failed to plead "direct evidence" in support of scienter); *Angelos v. Tokai Pharms., Inc.*, 494 F. Supp. 3d 39, 57–58 (D. Mass. 2020) (similar).

B. The Complaint's Allegations Regarding Post-Class Period Statements Does Not Support an Inference of Scienter

Instead of alleging facts showing the challenged statements were made with knowledge that they were misleading, or recklessly, the Complaint asserts that Defendants continued to mislead investors about the cause of vasculitis after the alleged class period. According to the argument, whose logic just begs the question, Defendants continued to speak falsely, and that shows their earlier statements must have been made with scienter. ¶¶ 118-49. The categories are: (1) statements about the potential cause of the post-approval vasculitis incidents, and (2) statements about the rate at which such incidents occurred.

As an initial matter, even assuming these statements about new events were false or misleading, that shows nothing about what facts were known to the Defendants at the time of their statements about the clinical trials. *In re Peritus Software Servs., Inc. Sec. Litig.*, 52 F. Supp. 2d 211, 228 (D. Mass. 1999) (plaintiffs must allege that the "relevant speakers knew, at the time of speaking, that their statements were false or misleading"); *see also In re Bos. Sci. Corp. Sec. Litig..*, 686 F.3d at 31 (complaint must generally contain "clear allegations of admissions, internal records or witnessed discussions suggesting that at the time they made the statements claimed to be misleading, the defendant officers were aware that they were

withholding vital information or at least were warned by others that this was so"). But the post-class period statements concern different subjects—potential causes of post-approval incidents of vasculitis and the rate at which such incidents occurred—not the absence of observed cases of vasculitis during the *pre-approval* clinical trials. They are thus irrelevant.[16] Finally, for the reasons below, these later statements were not false or misleading in any event.

1. Statements Regarding Potential Causes of Vasculitis

The Complaint first takes issue with statements concerning Defendants' theories of the potential cause of post-approval vasculitis incidents. ¶¶ 124–30. But Defendants cautioned that they did not know with certainty what caused the incidents and could not therefore have been speaking falsely. For example, the Complaint makes much of Defendants' warnings that physicians should discontinue use of a 19-gauge needle after Apellis observed manufacturing anomalies that it believed could have caused vasculitis. *Id*. But Defendants did not state that the needle was the established cause of the incidents; rather, they presented it as one potential cause based on a probabilistic analysis and an investigation of the structural differences between needles being used to administer injections.[17] These transparent statements about the analyses

[16] Plaintiffs apparently seek to suggest Defendants had a general propensity to lie, but this has not been shown (even remotely) and in any case would be insufficient to show scienter as to the relevant, challenged statements. *See Abiomed*, 778 F.3d at 245 ("[E]ven if the CWs' statements plausibly suggest that [company] was acting improperly, they do not show that defendants' statements about company policy and the FDA's inquiries were made with conscious intent to defraud or recklessly."); *Ezra Charitable Tr. v. Tyco Int'l, Ltd.*, 466 F.3d 1, 10 (1st Cir. 2006) ("It is ordinarily not sufficient to conclusorily allege 'an overarching fraudulent scheme or corrupt environment.'") (internal citation omitted).

[17] *See, e.g.*, Ex. 19 at 1 (noting that "[a] causal relationship has not been established" between these variations in needle and incidents of vasculitis); Ex. 20 at 6 (stating that use of the 19-gauge needle "*may explain* the[] cases of vasculitis," and that the theory was based on a "probabilistic analysis" that included some cases that were definitively linked to the 19-gauge needle and some cases from sites where both 18-gauge and 19-gauge needles were available). Apellis immediately discontinued use of the 19-gauge filter needle "out of an abundance of caution[.]" *Id*. (Sept. 6, 2023 earnings call transcript).

Apellis performed, made out of an abundance of caution to protect patients, could not lead investors to believe that the needle was the definitive cause.[18] Defendants similarly did not assert that the procedures to prepare injections definitively caused vasculitis, but again only stated that they "believe[d]" the effects "could be" related to the procedures, ¶ 120, a theory with which at least one opinion leader (cited by an analyst) agreed, ¶ 122 ("His initial guess is that the cause is associated with manufacturing or delivery . . . . "). To the extent that Plaintiffs disagree with those theories, that does not show falsity, much less that prior statements were made with scienter. *See Shash,* 84 F.4th at 17 ("[A] legitimate disagreement over scientific data does not give rise to a securities fraud claim"); *Pizzuto*, 2024 WL 1436025, at *9 (similar) (collecting authorities).

2. Statements Regarding the Observed Post-Marketing Rate of Vasculitis

Plaintiffs next point to post-class period statements regarding the observed rate of post-approval incidents of vasculitis. ¶¶ 124, 133–47. These allegations equally fail to show a false statement, as the statements were accurate and Defendants fully disclosed the basis for the rates. The Complaint first objects that Defendants presented the observed rate of vasculitis incidents "per injection" rather than "per patient." ¶¶ 133–34, 141–47. But having accurately described the statistic, Defendants were not obligated to provide some other statistic that Plaintiffs prefer.[19]

The Complaint also takes issue with the way Apellis estimated the number of injections administered, which Apellis based on the number of vials distributed at the time. ¶¶ 134, 141–42. The Complaint asserts that the number of vials distributed implies fewer injections than

[18] *See also* Ex. 1 at 9 (noting that Company would "need probably another quarter or 2 to really understand" whether recommendation against usage of 19-gauge needle "had an impact").
[19] *See Shash*, 84 F.4th at 17-18 ("The mere fact that [Defendants] engaged in [a particular] analysis cannot support a strong inference of scienter where [Defendants] did not mislead investors about the methodology employed") (citation omitted); *Kleinman*, 706 F.3d at 155-56 (objection to use of a particular analysis does not give rise to a strong inference of scienter).

Apellis estimated because vials distributed may not yet have been used and asserts that Apellis should not have included in the denominator injections made after the last-reported vasculitis incident.[20] As an initial matter, the Complaint fails to allege that Defendants had available to report any data other than vials distributed. But again, the statements had no capacity to mislead, because Defendants clearly disclosed the underlying basis for their estimate. For example (¶ 133), Defendants explained:

> All events were observed after the first injection of SYFOVRE, between 7-13 days after drug administration…The reported vasculitis events have occurred at ***an estimated rate of approximately 1 in 10,000 injections, or 0.01% per injection. To date, approximately 60,000 vials of SYFOVRE have been distributed since the U.S. Food and Drug Administration ("FDA") approval on February 17, 2023***.[21]

Finally, the Complaint focuses on Dr. Francois' statements during a November 28, 2023 analyst call, (¶¶ 146–47), in which he presented a statistic that was focused on cases of vasculitis that resulted in bad outcomes. The Complaint insinuates that he presented this different statistic (as opposed to a statistic about all cases of vasculitis) to misleadingly imply that the rate of vasculitis was lower than it was. But again, he clearly stated the basis for the statistic he was presenting. *See* Ex. 24 at 8 (Q: "So is that count[]ing only those patients adjudicated as vasculitis with bad outcomes? Or are you also counting nonvasculitis cases that had some visual exacerbation? A: No, that is vasculitis cases with bad visual outcomes, right? So that was . . .

[20] Even setting aside Defendants' transparency about the statistic, the latter point is nonsensical because it is obviously relevant to report the number of vials distributed and the number of injections made after the last observed incident of vasculitis without new incidents of vasculitis. Indeed, Plaintiffs would no doubt fault Defendants had they disclosed less.

[21] *See also* Ex. 18 at 1 (describing events as "very rare" in light of "68,000 commercial vials distributed and 23,000 clinical trial injections to date"); Ex. 19 at 1-2 (stating that "[t]o date, more than 100,000 vials have been distributed" and noting an "estimated real-world rate of 0.01% per injection"). Moreover, analysts demonstrated that they understood the statements. *See* Ex. 21 (July 17, 2023 Evercore Report) at 1 (noting estimated rate of "6 case[s] of vasculitis in 60K vials"); Ex. 22 at 1 (same); Ex. 23 (July 17, 2023 JP Morgan Report) at 1 (same).

on the denominator of 100,000 [injections]."). This was not misleading. *See supra* at 8. Analysts understood Dr. Francois' statements, and his forthrightness in explaining the statistics undercuts any inference of scienter. For all these reasons, the post-class period statements have no bearing at all on the scienter analysis here.

C. The Complaint's Remaining "Core Operations" Allegations Are Insufficient

The Complaint's remaining scienter allegations boil down to the contention that Defendants must have known about the alleged likelihood that pegcetacoplan would cause vasculitis because safety and the risk of vasculitis were important to pegcetacoplan's success, and pegcetacoplan's success was important to the Company's success (i.e., core operations). ¶¶ 157–67. As an initial matter, "core operations" is irrelevant. The doctrine, at best, is a response to an argument seen in other cases (but not here) by individual defendants that even where plaintiffs plead particular facts showing that a statement was false or misleading, they fail to plead that the individuals were aware of those facts. *See Leung*, 599 F. Supp. 3d at 66 ("Under such a theory, 'facts critical to a business's core operations . . . are so apparent that their knowledge may be attributed to the company and its officers.'") (quoting *Crowell v. Ionics, Inc.*, 343 F. Supp. 2d 1, 19 (D. Mass. 2004)). In other words, "core operations" argues that such knowledge can be inferred from the importance of the subject matter, which is an exception to the usual rule against pleading scienter by status. *See id.* But this has no place here—what Defendants argue is that Plaintiffs allege no facts showing any challenged statement was false or misleading in the first place.[22] *See DeMarco v. DepoTech Corp.*, 149 F. Supp. 2d 1212, 1232

[22] The Complaint similarly asserts that Defendants' experience with different adverse events from earlier clinical trials supports an inference of scienter. ¶¶ 150-54. This argument fails for the same reason as the "core operations" theory—Plaintiffs do not demonstrate that any challenged statement was false such that awareness can be inferred by the importance of the subject—but also because the adverse events *were not vasculitis*. *See id.* If anything, the absence of observed vasculitis in the earlier clinical trial only bolsters the competing inference—

(S.D. Cal. 2001) (absent falsity, scienter analysis "entails the illogical inquiry into whether the defendant intended to deceive when, in fact, there was no deception").[23]

IV. The Complaint Fails to Plead Control Person Liability

Having failed to plead a primary violation, Plaintiffs' Section 15 and Section 20(a) "control person" claims fail as well. *ACA Fin. Guar. Corp.*, 512 F.3d at 67 ("The plain terms of section 20(a) indicate that it only creates liability derivative of an underlying securities violation."); *Kader*, 2017 WL 72396, at *8 n.6 (same).

CONCLUSION

For the foregoing reasons, the Complaint should be dismissed with prejudice and without leave to amend.

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that Defendants had no reason to believe that there was a heightened risk of vasculitis with respect to DERBY and OAKS, or otherwise.

[23] In any case, courts "have refused to apply this doctrine absent other significant evidence of a defendant's intent or recklessness, or a 'plus factor.'" *Quinones v. Frequency Therapeutics, Inc.*, 665 F. Supp. 3d 156, 180 (D. Mass. 2023) (internal citations omitted); *In re Psychemedics Corp. Sec. Litig.*, 2017 WL 5159212, at *6 (D. Mass. 2017) (dismissing where "theory st[ood] naked, unadorned by any other piece of evidence purporting to establish the essential 'plus' factor—guilty knowledge on the part of [the Defendants]"); *see also Pizzuto*, 2024 WL 1436025, at *18 (similar). Here, the Complaint alleges none.

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Respectfully submitted,

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